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EXAMINER	
LEITH, PATRICIA A	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/774,092	BROVELLI ET AL.	
	Examiner	Art Unit	
	Patricia Leith	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 October 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3,6,7 and 23-26* is/are pending in the application.

4a) Of the above claim(s) *26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3,6,7 and 23-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 3, 6-7 and 23-26 are pending in this application.

Claim 26 remains withdrawn from examination on the merits as being directed toward a non-elected invention as established in the previous Office action.

Claims 3, 6-7 and 23-25 were examined on their merits.

Rejections/Objections Removed

The previous objection to claims 3 and 23 are hereby removed due to Applicants' amendment to these claims removing language pertaining to performing an extraction.

The previous rejection of claims 3, 6-7 and 23-25 under 35 USC 112 Second paragraph are removed due to Applicants' amendment to claim 3 removing the language 'at least about' and further, for amending the claims to replace 'determining optimal harvest window' with – selecting a maturation stage—and for inserting 'that has both' into claims 3 and 24.

The previous rejection of claims 3, 6-7 and 23-25 under 35 USC 112 First paragraph are hereby removed due to Applicants' amendments to the claimed invention. Applicants removed the term 'at least about' from claims 3 and further amended claims 3 and 24 to replace 'determining optimal harvest window' with – selecting a maturation stage—. However, a new 112 Rejection based upon Applicants' amendments to the claims has been instituted *infra.*

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3, 6-7 and 23-25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The MPEP states that the purpose of the written description requirement is to ensure that the invention had possession, as of the filing date of the application, of the specific subject matter later claimed by him or her. The courts have stated:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that the inventor invented the claimed invention.' Lockwood v. American Airlines, Inc., 107 F. 3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); In re Gostelli, 872 F. 2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, no that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F. 3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient" MPEP § 2163.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP § 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus MPEP § 2163. Although the MPEP does not define what constitutes a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad generic. *In Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618. .

The description requirement of the patent statue requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736, F. 2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outline [goals] appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.") Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed had possession of the entire scope of the claimed invention.

Specifically, claims 3 and 24 have been amended to read '(i) a standardized concentration of about 3.26% to about 3.62% of chicoric acid…'. The disclosure, as filed, does not support this new limitation. While 7 specific percent values for chicoric acid are given in Table 1, Applicants do not disclose any levels between these values, nor do they teach explicitly or implicitly that the values may be 'about' these amounts. Therefore, 'about 3.26% to about 3.62%' is considered New Matter.

Because claims 6-7 and 24-25 depend directly or directly upon either of claims 3 or 23 respectively and because these claims do not remedy the deficiencies of either of claims 3 or 23 respectively under this statute for lacking written description, these claims also comprise new matter and are properly rejected under this statute.

In order to overcome this rejection, Applicants are required to either delete the new matter in claims 3 and 23 or provide convincing evidence and/or arguments to establish that the limitation in question is present either explicitly or implicitly within the disclosure as filed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 3, 6-7 and 24 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Gahler et al. (US 6,511,683) in view of Letchamo et al. FACTORS

AFFECTING ECHINACEA QUALITY; ASHS Press, Alexandria, VA (2002), Seidler – Lozykowska et al. (2003), Dou et al. (2001 – Abstract) and Rininger et al. (2000) .

Gahler et al. . (US 6,511,683) recognized the advantage of standardizing extracts of Echinacea for several desired endogenous compounds such as chicoric acid, alkylamides and polysaccharides (see entire patent and Abstract):

> [I]t is desirable to formulate Echinacea compositions to contain standardized amounts of biologically active components derived from Echinacea plants. Such standardized, Echinacea compositions provide the consumer with a consistent, effective dose of one or more, biologically active, Echinacea components. In particular, there is a strong commercial market for Echinacea extracts containing a high concentration of one or more, biologically active, Echinacea components believed to promote good health. Such highly enriched extracts can be used directly as dietary supplements, or can be blended with other Echinacea extracts to prepare dietary supplements containing standardized amounts of biologically active, Echinacea components. (col. 1, lines 23-37)

Gahler et al. clearly established the desirability of standardizing Echinacea for several markers in order to produce extracts with added medicinal benefit (see column 1):

> Scientific studies indicate that Echinacea-derived polysaccharides, alkylamides and chicoric acid (a caffeic acid derivative also known as chicoric acid, 2,3-o-di-caffeoyl-tartaric acid) each possess health-promoting properties. For example, alkylamides from Echinacea have been shown to stimulate phagocytosis in mice granulocytes at concentrations of about 0.1 parts per million (ppm). Bauer, R. et al., Arzneim.-Forsch./Drug Research, 38: 276-281 (1988). Similarly, chicoric acid has been shown to increase phagocytosis in granulocytes, and may stimulate the immune system at concentrations as low as 0.01 ppm. See e.g., A. Awang et al., supra. Echinacea polysaccharides have been shown to inhibit hyaluronidase, increase phagocytosis, induce the release of interferon-6, and enhance resistance to C. albicans infection in mice. See, e.g., A. Awang et al., supra; Wagner, H, et al. Arzneim.-Forsch./Drug Research, 35: 1069-1075 (1985).

> (7) Numerous factors must be considered and optimized in order to produce Echinacea extracts having a high concentration of polysaccharides, alkylamides and/or chicoric acid. For example, the amounts of polysaccharides, alkylamides and chicoric acid in Echinacea plants are influenced by the species of the plant, the age of the plant and the plant growth conditions. Additionally, the solvents and process parameters, such as temperature and length of extraction period, utilized to extract polysaccharides, alkylamides and chicoric acid from Echinacea plants can greatly affect the yield of these components.
>
> (8) Thus, there is a need for methods for efficiently extracting polysaccharides, alkylamides and chicoric acid from Echinacea plants, and for Echinacea extracts containing a high concentration of polysaccharides, alkylamides and/or chicoric acid. Further, there is a need for standardized Echinacea compositions containing a predetermined, desired amount of Echinacea extracts, including polysaccharide, alkylamide and/or chicoric acid extracts.

Gahler et al. additionally recognize the importance of selecting an Echinacea plant at a particular growth stage with the desired amounts of each analyte marker compound (see col. 2, and columns 11-12 for example). Here, Gahler et al. provides detailed information of how to select Echinacea for optimum analyte concentration.

Gahler et al. clearly established that their extracts containing multiple marker compounds influenced immune system parameters such as IL-2 and TNF-α (*inter alia*) (see, for example, Figures 1-7 and 'Brief Description of the Drawings').

Gahler et al. did not specifically teach where Echinacea plants were harvested at different maturation stages and added to a cell culture to analyze immune products or translation products induced by Echinacea, or wherein a stage of maturation was

selected which had a standardized concentration of 'about 3.26 to about 3.62% chicoric acid' and the highest observed level of immune-stimulatory product.

Letchamo et al. FACTORS AFFECTING ECHINACEA QUALITY; ASHS Press, Alexandria, VA (2002) teach that Echinacea is "…among the most frequently utilized medicinal herbs around the world" known for treating cold, cough and sore throats (p. 514). Letchamo et al. indicate that the pharmacological activity/chemical content of common markers (such as chicoric acid)of Echinacea extracts vary significantly upon choice of soil selection, disease, insect infestation, climate, country of origin and harvest time (see entire reference, especially p. 514, 515, Table 1, , Table 3, and Table 4). Letchamo et al. show that chicoric acid content as a percentage of dry matter varies with regard to the country of origin, with Russian cultivars producing the highest yields of chicoric acid (Table 1). Letchamo et al. clearly demonstrate the nexus between harvest time and chicoric acid content: Table 4 reports the effects of flower developmental stages on chicoric acid content. Table 4 demonstrates that chicoric acid levels of *E. purpurea* at the early flower developmental stages produce the optimum amount of chicoric acid of 3.97% (see Table 4). The authors establish that they suggest that a 2.2% level of chicoric acid concentration for any standardized *E. purpurea* material (see p. 520 under Conclusions).

Echinacea was well known in the art for imparting immunological activity of macrophage cells according to Rininger et al. (2000). Specifically, Rininger et al. analyzed the production of TNF- α, IL-1α, IL-1βIL-6, IL-10 and nitric oxide from macrophage cells upon contact with several products of Echinacea including standardized extracts, whole plant material, juice and phenolic compounds (see entire reference, especially pages 4-10). Rininger et al. specifically stated that "Echinacea immunostimulatory activity varied significantly from lot-to-lot of raw material from the same supplier and may reflect growth conditions, time of harvest, milling and storage conditions" (p. 10).

Seidler – Lozykowska et al. (2003) analyzed the polyphenolic acid content of Echinacea purpurea during various growth stages of the plant (see Abstract and Material and Methods). Seidler – Lozykowska et al. determined that "the highest concentration [of polyphenolic acids] was in the leave blades…during flowering stem formation in one year plants".

Dou et al. (2001- Abstract) taught assaying the level of chicoric acid in *Echinacea purpurea* plant material in different stages of growth (see Abstract). Dou et al. indicated that "The content of chicoric acid and yield were the highest in the overground part of *E. purpurea* before and after the bloomy stage" (Abstract).

The desirability of creating Echinacea extracts with increased immunopotentating activity, as well as increased levels of compounds such as chicoric acid was *well-documented in the art* (see cited references, especially Gahler et al.). It is deemed that the method claims of the Instant invention would have been well-within the purview of the ordinary artisan at the time the invention was made having the above-cited references before him or her. One of ordinary skill in the art would have had a reasonable expectation of success in choosing an Echinacea plant with 'the highest' amount of immuno-stimulatory' activity and at least some amount of chicoric acid because both immuno-stimulatory activity as well as chicoric acid were desired at the time the invention was made.

One of ordinary skill in the art would have been motivated to harvest Echinacea at different growth stages to ascertain its immunopotentiality on macrophage cells in order to assess immuno-function of the plant at different stages. Analyzing Echinacea plants at different stages for particular immuno-potentiating compounds was known in the art according to Letchamo et al., Dou et al. and Seidler – Lozykowska et al. (2003), and Rininger et al. recognized that the variance of immunostimulatory activity was probably due to time of harvest *inter alia.* Thus, the ordinary artisan would have had a reasonable expectation that testing the Echinacea at varying growth stages for immunopotentating activity would have determined an optimum harvest time for the Echinacea.

It is clear from Rininger that what was investigated was immunostimulatory activity of Echinacea; via quantitatively assessing transcriptional products (cytokines) produced by RAW 264.7 cells in response to contact with Echinacea. Therefore, what was known in the art at the time the Invention was made was that Echinacea had immunostimulatory properties which were scientifically investigated. What was further known in the art was that Echinacea could be tested *in-vitro* for immunopotentating ability by measuring transcriptional products such as TGF and IL produced by RAW 264.7 cells. Therefore, it was well known at the time the Invention was made that amount of these transcriptional products produced by RAW 264.7 cells were proportional to the plant's immuno-potentiating activity (see Rininger et al., Figures 1 and 2 for example). Rininger et al. further specifically stated that that "Echinacea immunostimulatory activity varied significantly from lot-to-lot of raw material from the same supplier and may reflect growth conditions, time of harvest, milling and storage conditions" (p. 10). Again, analyzing Echinacea plants at different stages for particular immuno-potentiating compounds and chicoric acid was well-known in the art . Therefore, the ordinary artisan would have been motivated to determine the optimal harvest window of Echinacea in order to obtain plant material which possessed maximum immunopotentating effects.

It is noted that the prior art does not specifically teach all of the claim limitations in one reference, hence, there is no 102 rejection. However, the invention as a whole is rendered obvious by the prior art references. Echinacea plants were well-known in the

art at the time the invention was made and exhaustively studied for their medicinal effects. The claimed invention as a whole is obvious, and there is no individual step in any of the method claims which was not already known or made obvious by the prior art. That is, there is no novel step or idea in the method claims which makes it unobvious over the prior art references. According to the prior art references, as keenly pointed out in the previous Office actions, Echinacea plants were known to be studied at different maturation stages for marker compounds to select for optimum levels of compounds. Echinacea plants were also known to contain immunopotentating activity, and these activities were known to be studied and already determined to depend, in part, upon the harvesting time of the Echinacea. Harvesting Echinacea plants in the vegetative stage was known, due to the level of chicoric acid in the flowers at this stage of plant maturation. Additionally, Applicants' method for determining the level of immunopotentating activity, as well as marker immuno stimulatory products were known in the art at the time the invention was made. While no one, individual reference taught all of these steps together; the ordinary artisan would have been motivated to perform the claimed method in order to optimize medicinal efficacy of an Echinacea extract and standardization would have been routine in manufacturing extracts with essentially uniform chemical constituents and hence, medicinal effectiveness: *"[a] person of ordinary skill is also a person of ordinary creativity, not an automaton* *KSR* 127S. Ct. at 1742 (emphasis added).

. Letchamo et al. makes plainly evident that that selection of marker compounds such as chicoric acid present within the claimed range ('at least about 3.40%) were already known in the art through their routine experimentation to test chicoric acid levels in different maturation stages of Echinacea plant growth. Letchamo et al. further offer that chicoric acid should be standardized to at least 2.2%. Hence, while Applicants found that in their investigation, a particular plant of Echinacea purpurea at the vegetative stage contained 3.49% of chicoric acid and the maximum amount of immunopotentating activity; this data is not found to be significant and is not considered to be reproducible considering that Applicants did not disclose specific growing conditions of Echinacea; in other words, the chicoric acid content and immunopotentating activity will inevitably be different from plant to plant. It is expected that different maturation stages of Echinacea will produce optimum amounts of chicoric acid and optimum results when assayed for immunopotentating activity. As reiterated throughout this prosecution, it is evident that in Applicants' study, the level of chicoric acid was relatively consistent throughout maturation stages. Now, as claimed, the method requires that a maturation stage is selected which comprises about 3.26 to 3.62% of chicoric acid and a highest level of immune-stimulatory product. The claims are deemed obvious and well-within the skill level of the ordinary artisan at the time the invention was made.

It is deemed that the method as claimed is an obvious variation of known methods to produce extracts of Echinacea having maximum amounts of chicoric acid

and immuno-potentiating effects. To arrive at the claimed invention would have been well-within the purview of the ordinary artisan having the above- cited references before him or her, and could have been achieved through routine experimentation.

Response to Argument

Applicants' arguments present on pp. 5-9 concerning the rejections which have been removed (see *supra*) are moot. As stated *infra*, these rejections were removed due to Applicants' amendments to the claims in order to overcome said rejections.

With regard to the 103(a) rejection above, Applicants argue:

> In contrast, the disparate references cited by the Examiner all point to a process for harvesting the Echinacea plant at a selected stage where the amount of a certain marker, typically chlorogenic or chicoric acid, can be standardized at a desired level. Obviously, the art recognizes that certain regions of the world and certain harvest times will lead to plants containing a different amount of the marker. Such a recognition, however, does not teach or suggest to one of skill in the art that they should also analyze the same Echinacea plant for a level of an immune-stimulatory product and select the particular maturation stage that has the required concentration (i.e., about 3.26% to about 3.62%) of chicoric acid and the highest observed level of the immune- stimulatory product.
>
> While it is true that it was known in the art to test Echinacea and Echinacea extract to determine if it exhibited immunostimulatory activity (Rininger), there is no teaching or suggestion that one of skill in the art would use such information together with a determination of a concentration of chicoric acid in an amount between about 3.26% to about 3.62% to select a maturation stage. At best, one of skill in the art upon reviewing Rininger would merely conclude that if one sought to use Echinacea for immunostimulatory activity, one of skill in the art should use the whole herb or root powder and not a standardized extract. This teaching is different from and not related to the present method which seeks to select a particular maturation stage based both the standardized concentration of chicoric acid (at a specified level, i.e., from about 3.26% to about 3.62%) and the highest observed level of immune-stimulatory product

Applicants' statement that the cited references are disparate has not been verified by cooberating, convincing argument. Applicants' statement appears to be unreasonable considering that all of the references cited by the Examiner relate to medicinal compounds used as markers to standardize Echinacea preparations. Hence,

Applicants assertion that the cited references are disparate is unsubstantiated and not found convincing.

The prior art clearly recognizes the advantages of standardizing Echinacea for multiple marker compounds such as chicoric acid and immune-stimulating polysaccharides (Gahler et al., *Id.*) Although the prior art does not teach Applicants' claimed range of chicoric acid, the claimed range of 'about 3.26 to about 3.62' is obvious considering that chicoric acid levels within this range were already known in the art (Letchamo et al., *Id.*). Hence, Applicants' claimed method is deemed obvious from the teachings of the prior art. Applicants determined concentrations of chicoric acid in a plurality of maturation stages of Echinacea, to find that the level of chicoric acid remained relatively constant. Applicants' selection of maturation stage was thus primarily based upon finding the greatest level of immune stimulation via *in-vitro* assay. Applicants' methods as claimed are decidedly *a priori* obvious considering the teachings in the prior art which clearly indicate that marker compounds such as chicoric acid and polysaccharides (immunopotentiators) from Echinacea were highly sought-after compounds for standardizing Echinacea preparations such as extracts. Hence, selecting a maturation stage of Echinacea with optimal concentrations of a plurality of marker compounds such as chicoric acid and immunopotentating activity would have been *prima facie* obvious to one of ordinary skill in the art at the time the Invention was made in light of the references.

Applicants argue "At best, one of skill in the art upon reviewing Rininger would merely conclude that if one sought out use Echinacea for immunostimulatory activity, one of skill in the art should use the whole herb or root and not a standardized extract…" (p. 10, Remarks). However, In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). It is the *combination* of references which renders the claimed invention obvious. Rininger is relied upon in the outstanding 103(a) rejection because this reference teaches that testing Echinacea products for immunopotentiating activity *in-vitro* using cell culture assays was well-known and conventional practice. Rininger additionally provides for the fact that marker compounds present in Echinacea vary between lot-to-lot depending upon characteristics such as harvest time (i.e., harvesting at different maturation times). Additionally, Applicants are reminded that the claimed invention no longer recites preparing a standardized extract and thus, preparation of such an extract is not required by the claims and does not set the invention apart from the combined teachings of the prior art.

Testing for chicoric acid levels at different maturation stages was known in the art and immunopotentating activity had already been linked to harvest time. One of ordinary skill in the art would readily recognize from the prior art that Echinacea plants contain immuno potentiating activity; whether it be manifested from polysaccharides or

alkylamides or some other endogenous phytochemical in Echinacea (e.g., see Fig. 5 of Gahler and Col. 4, lines 48-58) and that these phytochemicals would be present in the Echinacea plant.

The Echinacea plant chosen in Applicants' method claims will have immuno-potentiating activity, because the *plant contains all of the immuno-potentiating compounds*. The ordinary artisan, having the above-cited references before him or her, and thus possessing the knowledge that Echinacea comprises highly sought-after chicoric acid as well as immuno-potentiating activity would have been motivated to determine the optimal maturation stage of their Echinacea crop based upon cell assays on various harvest times to determine immunopotentating activity and chicoric acid content to maximize immunopotentating activity and chicoric acid content. One of ordinary skill wishing to do this, might be interested in selling the plant whole; e.g., as in a dry powder form. Again, the claim is directed toward selection of a particular maturation stage . The ordinary artisan, having the above-cited references before him or her would have had a reasonable expectation of success in using the claimed invention to ascertain their own optimal maturation stage seeing that 1) Echinacea was known to be tested at various levels for chicoric acid content and 2) that Echinacea was known to have immuno potentiating activity and that this immuno potentiating activity was known to be tested via monocyte cell culture for cytokines such as IL-1 (see Rininger).

The techniques found in the claims; e.g., assaying for chicoric acid levels and cell assays to determine amounts of immuno-products produced from cell assays with regard to Echinacea were well-known in the art. Optimizing harvest times based upon chicoric acid content was well-known in the art and Rininger specifically suggested that immunopotentating activity was affected by harvest time. Hence, having the knowledge of the prior art, one of ordinary skill in the art, wishing to obtain an optimal harvest time of Echinacea would have been motivated to perform the claimed method steps. And to reiterate from above, although each method step was not explicitly taught in one prior art reference; considering the knowledge pertaining to Echinacea as set forth keenly *supra*, it is determined that the claimed method steps could have been achieved through routine optimization of prior art methods for determining optimal harvest time of Echinacea. Hence, respectively, in the opinion of the Examiner, there is nothing within the claimed invention that rises above the conventional knowledge concerning harvesting Echinacea plants for marker compounds which would be rendered patentable.

"Common sense teaches … that familiar items may have obvious uses beyond their primary purposes, and in many cases a person or ordinary skill will be able to fit the teachings of multiple patents together like pieces of a puzzle." *KSR*, 127 S.Ct. at 1742. *See also, Muniauction, Inc. v. Thomson Corp.*, ___ F.3d ___, 2008 WL 2717689, at *6-*10 (Fed. Cir. July 14, 2008); *Leapfrog Enterprises, Inc. v. Fisher-Price, Inc.*, 485 F.3d 1157, 1160-63 (Fed. Cir. 2007).

The Supreme court has acknowledged that:

> When a work is available in one field of endeavor, design incentives and other market forces can prompt variations of it, either in the same field or a different one. **If a person of ordinary skill can implement a predictable varition..103 likely bars its patentability**…if a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond that person's skill. A court must ask whether the improvement is more than the predictable use of prior-art elements according to their established functions…

…**the combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results** (see *KSR International Co. v. Teleflex Inc*., 82 USPQ2d 1385 U.S. 2007) emphasis added.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia Leith whose telephone number is (571) 272-0968. The examiner can normally be reached on Monday - Friday 8:30am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terry McKelvey can be reached on (571) 272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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